



Patent

Attorney's Docket No. 020600-285

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
SCHMIDT et al) Group Art Unit: 1655
Application No.: 09/462,635) Examiner: J. Goldberg
Filed: April 10, 2000)
For: CATEGORISING NUCLEIC ACID)
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AMENDMENT AND REPLY

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In complete response to the Official Action mailed on May 18, 2001, applicants provide the following amendments and remarks.

In The Claims:

Please cancel claims 4-5, 7-12, 23-41 and 50-63, without prejudice or disclaimer to the subject matter disclosed therein.

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the above-identified application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

By the foregoing amendment, claims 4-5, 7-12, 23-41 and 50-63 have been canceled, without prejudice or disclaimer to the subject matter disclosed therein. Applicants of course reserve the right to pursue the subject matter of the canceled claims in a continuation application. The pending claims are claims 14-22 and 42-49. No new matter has been added by the present amendment.

In light of the cancellation of these claims, the only remaining rejections of the claims are a rejection of claims 14-22, 42-46 and 49 under 35 U.S.C. § 103(a) (for purportedly being unpatentable over Rothberg et al in view of Dynal Catalog) and a rejection of claims 47-48 under 35 U.S.C. § 103(a) (for purportedly being unpatentable over Rothberg et al in view of Dynal Catalog and further in view of Hartley et al). Each of these rejections are discussed in detail below.

Rejection of Claims 14-22, 42-46 and 49 Under 35 U.S.C. § 103(a)

Claims 14-22, 42-46 and 49 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Rothberg et al (U.S. Patent No. 5,871,697) in view of Dynal Catalog (1995). For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

The pending claims are drawn to a method for categorizing nucleic acid. The method comprises digesting double-stranded nucleic acid with an endonuclease to produce a nucleic acid population. Each nucleic acid in the nucleic population produced has a sticky end of a known base sequence and common length and a double-stranded portion. An adaptor is then ligated to the terminal of each nucleic acid in the population. The

nucleic acids in the nucleic acid population are then categorized by isolating a nucleic acid wherein both termini of the double-stranded portion of the nucleic acid correctly hybridize to an oligonucleotide sequence.

Rothberg et al and Dynal Catalog, either alone or taken together, do not disclose or suggest the methods of the pending claims. In particular, neither of the cited references disclose or suggest that both termini of the double-stranded portion of the nucleic acid in the nucleic acid population correctly hybridizes to an oligonucleotide sequence. This feature is illustrated in Figures 4 and 5 of the application as filed. These figures show the first set of oligonucleotide sequences and the second set of oligonucleotide sequences hybridize to different termini of the double-stranded portion of nucleic acid, and that both the oligonucleotide sequences of the first and second sets each comprise a region which recognizes a portion of the nucleic acid which was double-stranded after digestion with the endonuclease. Thus, neither of the prior art references suggest a method wherein nucleic acid is categorized according to the sequence of both ends of the double-stranded portion.

The Examiner states that the ordinary artisan would be motivated to perform a categorizing method according to Rothberg et al and subsequently perform the method of the Dynal Catalog. However, the ordinary artisan would not arrive at the invention as claimed in the pending claims by simply performing the method of the Dynal Catalog after the method of Rothberg et al. The individual steps of each of the methods would need to be combined, at least in so far as to the selection of the timing of immobilization of the nucleic acid was concerned, in order to arrive at step (iii)(e) of claim 14, and there is not suggestion or motivation to combine these steps. Therefore, one of skill in the art would

not simply arrive at the method of claim 14 by annexing the method of the Dynal Catalog to that of Rothberg et al. Furthermore, as mentioned above, there is no suggestion in either of these references both termini of the double-stranded portion of the nucleic acid in the nucleic acid population correctly hybridizes to an oligonucleotide sequence (see claim 14, step (iii)). Thus, even if the methods were combined, the resulting method would still be missing that key feature of claim 14.

The Examiner appears to suggest that the motivation of the skilled artisan for combining the teaching of the two prior art references would be in order to generate single-stranded probes of known sequences which then could be identified by the categorization method of Rothberg et al. The Examiner also purports that Rothberg et al discloses that any amplification method that selects fragments to be amplified based on end sequence is adaptable, and that therefore the method of the Dynal Catalog should be considered an equivalent means of amplifying the DNA fragments. The Examiner appears to view the disclosure of the Dynal Catalog as simply an amplification method which would be used before or after the categorization method of Rothberg et al.

Contrary to the Examiner's suggestion, there are very good reasons as to why the skilled artisan would have no motivation to combine the disclosures of Rothberg et al and the Dynal Catalog, even if such a combination would arrive at the invention as defined in the pending claims (which it does not). The Dynal Catalog does not relate to a method of amplifying DNA. Rather, the Dynal Catalog relates to a method for producing labeled single-stranded probes from double-stranded DNA for applications such as *in situ* hybridization.

In the present invention, the steps involving immobilization of nucleic acids on a solid phase (see steps (iii)(b) to (h) of claim 14) are not performed in order to amplify the DNA as such, but are part of the categorization process. The immobilization feature contributes to the method by allowing the use of more stringent washing and hybridization conditions. There is no suggestion in Rothberg et al that the nucleic acids should be immobilized or that the categorization process should be performed as defined in claim 14. Rothberg et al refers only to standard amplification methods, and not for those involving immobilization of DNA or categorization according to claim 14.

In light of these remarks, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

Rejection of Claims 47-48 Under 35 U.S.C. § 103(a)

Claims 47-48 have been rejected under 35 U.S.C. § 103(a) for purportedly being unpatentable over Rothberg et al (U.S. Patent No. 5,871,697) in view of the Dynal Catalog (1995), as applied above, and further in view of Hartley et al (U.S. Patent No. 5,106,727). For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

As discussed in more detail above, Rothberg et al and the Dynal Catalog, even if taken together, do not disclose or suggest the claimed invention. Hartley et al does not solve the deficiencies of Rothberg et al and the Dynal Catalog. Specifically, Hartley et al does not disclose or suggest a method of categorizing nucleic acids wherein both termini of the double-stranded portion of a nucleic acid in a nucleic acid population correctly

hybridizes to an oligonucleotide sequence. Therefore, Hartley et al does not solve the deficiencies of Rothberg et al and the Dynal Catalog, and even if the disclosures of these three references were taken together, the present invention would not be *prima facie* obvious in view of the combined disclosures.

In light of these remarks, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

In the event that there are any questions relating to this application, the Examiner is invited to telephone the undersigned attorney so that prosecution of the subject application may be expedited.

Respectfully submitted,

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